Conservative Treatment of Early Breast Cancer

Long-term Results of 1232 Cases Treated with Quadrantectomy, Axillary Dissection, and Radiotherapy

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One thousand two hundred and thirty-two women with invasive breast cancer lesions measuring less than 2 cm in diameter, clinically assessed as $T_1N_{0-1}M_0$, were treated from 1970 to 1983 at the National Cancer Institute of Milan with quadrantectomy, axillary dissection, and radiotherapy (QUART). Pathologic evidence of lymph-nodes metastases was found in 32% of the patients. Overall survival at 5 and 10 years from surgery was 91% and 78%, respectively. The cumulative probability of survival tends to decrease with increasing tumor size: the 7-year survival rate was 84% in cases in which lesions measured from 1.6 to 2.0 cm, and 94% in cases in which the lesions were less than 0.5 cm. Tumor site in the treated breast did not affect distant outcome. No difference was found between the patients without node metastases and patients with one node involved, whereas the patients with more than one node showed a lower probability of survival. The survival curves of 352 cases treated inside a randomized trial and that of 880 cases routinely treated appear to be superimposable. Local recurrences and new primary ipsilateral tumors were, respectively, 35 (2.8%) and 19 (1.6%); 56 women with local recurrences or second tumors underwent second surgery (total mastectomy, 43; wide resection, 11). Five of them died from distant spread of breast cancer, while 49 are alive and well. In the contralateral breasts 45 carcinomas were recorded during the follow-up time. The results of the present analysis of a large number of T_1 cases reconfirm the safety of integrated radiosurgical conservative treatments.

EDUCATIONAL CAMPAIGNS, screening programs, and progress in early diagnosis have radically changed the characteristics of breast cancer patients we see today compared to those observed in the past. Twenty years ago only a minority of patients presented with tumors of less than 2 cm, while today approximately 40% of treated cases are small cancers, at least in developed countries, and a further improvement is expected in the future. These are the main reasons for the development of breast conservation programs in the treatment of mammary carcinoma. Other factors were the failure of aggressive superradical surgery, new concepts concerning the natural history of breast cancer, and the increased patient demand for less mutilating surgery.

The first randomized trial aimed at the preservation of the breast was carried out in London in the 1960s, but the results were not encouraging because they showed that patients treated with breast resection (without axillary dissection) and radiotherapy at the dosage of 30 to 38 Gy experienced a higher number of locoregional recurrences and a lower survival rate than those treated by Halsted's mastectomy.[1]

The first controlled study showing that a conservative treatment (quadrantectomy, axillary dissection, and radiotherapy with a dosage of 60 Gy) compares favorably with the Halsted mastectomy was performed at the Milan Cancer Institute, the first results of which were published in 1981.[2] In this trial, 701 patients with breast tumors of less than 2 cm in diameter, without clinical axillary involvement, were randomized into one of the two treatment groups. The results after 12 years showed no statistical difference between the mutilating and the conservative treatment, both in terms of survival and local control of the disease.[3] The trial stressed the safety of this new conservative radiosurgical procedure as an alternative to radical mastectomy in the treatment of breast cancers of small size.

The results of a French trial, published in 1983,[4] and of an American trial, published in 1985,[5] confirmed the reliability of this therapeutic approach.

After the publication of the Milan study, quadrantectomy and other nonmutilating operations were extensively introduced into surgical practice in most western countries. At the Milan Cancer Institute, by the end of 1987,

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more than 4000 patients had been treated with a limited, conservative procedure.

The aims of this paper are (1) to measure the survival probability of a series of 1232 consecutive patients, homogeneously treated with breast preserving therapy (QUART) according to a number of variables related to age of patients, characteristics of primary tumor, and axillary nodes; (2) to record unfavorable events (local recurrences, second primary breast carcinomas, contralateral carcinomas, distant metastases); (3) to compare survival of patients treated inside a clinical randomized trial to that of patients treated routinely, outside any clinical trial; and finally (4) to consider the possible oncogenic risk of radiotherapy.

Patients and Methods

One thousand two hundred and thirty-two women with invasive breast cancer of less than 2 cm in diameter, clinically assessed as $T_1N_{0-1}M_0$, were treated from 1970 to 1983 at the National Cancer Institute of Milan with quadrantectomy, axillary dissection, and radiotherapy (QUART). This case series consists of 352 patients treated with QUART in a clinical trial comparing this procedure to Halsted's mastectomy (1973 to 1980) and 880 patients routinely treated with the same procedure outside the trial, mostly after the closure of trial patients's accruals.

The main characteristics of the whole series are shown in Table 1. In all patients the largest lesion diameter was 2 cm or less. Pathologic evidence of lymph-node metastases was found in 32% of the patients. In most cases one node was involved and only in 2% of cases were more than 10 nodes metastatic.

TABLE 1. *Main Characteristics of the 1232 Patients*

Variable	Number	%
Site of Primary Tumor		
Outer quadrants	824	67
Inner quadrants	408	33
Age at Surgery (years)		
≤35	95	8
36–45	385	31
46–55	401	32
>55	351	28
Pathologic Size (cm)		
≤0.5	91	7
0.6–1.0	430	35
1.1–1.5	396	32
1.6–2.0	257	21
Not evaluable	58	5
Axillary Nodal Metastases		
Absent	842	68
Present	390	32
1 Node	198	51
2–3 Nodes	109	28
>3 Nodes	83	21
Postmenopause	496	40
Histologic Type		
Ductal infiltrating	920	75
Lobular infiltrating	163	13
Others	149	12

The Quadrantectomy

Quadrantectomy is a term coined by one of us (U.V.), to define an operation consisting of the complete removal of the breast quadrant harboring the primary cancer,[6,7] including the skin and the superficial fascia of the major pectoralis muscle. The incision of the skin is elliptical with the major axis radial from the nipple.

In all cases a complete axillary dissection was performed in continuity when the tumor was located in the breast tail. In the other cases, the dissection was done in discontinuity, mainly with an anteroposterior incision crossing the axillary fossa in a downward direction.

Radiotherapy

Radiotherapy, as an integral part of the conservative treatment, was given in all cases starting 3 to 6 weeks after the operation and was limited to the ipsilateral breast tissue. As a rule, the regional axillary, supraclavicular, and internal mammary nodes were not irradiated. The breast tissue was irradiated with either a linear accelerator or with a cobalt^{60} unit. The two opposing tangential fields had an extension wide enough to cover the breast and the adjacent tissues. The fields were 16 to 20 cm long and 8 to 12 cm wide. The lateral limit of the external tangential field overlapped the medial axillary line, while the medial limit of the internal tangential field was set 2 cm beyond the middle sternal line. When the breast tissue was of limited volume the two tangential fields allowed a dosage sufficiently homogeneous to the whole breast. When the breast was large and very prominent, it was necessary to use wedge filters to obtain a homogeneous distribution of the dosage.

The daily dosage, calculated at the breast midplane, was 2 Gy, administered with the daily use of both opposite fields. With five weekly sessions, the requested dose of 50 Gy was reached in 5 weeks. During the sixth week an overdose was delivered through a field of approximately 12×8 cm around the tumor bed, with Roentgen therapy, or with 10-MeV electrons.

The treatment was well tolerated, without serious myelodepression, so that adjuvant chemotherapy, whenever indicated, could be administered at the normal doses.

Adjuvant Treatments

Of 390 patients with positive nodes, 271 (78.5%) received adjuvant systemic chemotherapy, which consisted of CMF regimen for 12 months (196 cases) or 6 months (32 cases), or CMF combined with Adriamycin in an al-

ternating scheme (43 cases); 23 patients with positive nodes did not receive chemotherapy but adjuvant radiotherapy on regional nodes, 45 patients did not receive any adjuvant treatment, while 19 postmenopausal patients received only tamoxifen for 1 year.

Data Collection and Statistical Methods

Data were carefully controlled by means of computer interactive programs. A team of surgeons and data managers updated in real time the follow-up of patients.

Death from all causes, first local failure, and distant metastases were taken as endpoints; times to each of these events were measured from the date of surgery. Patients lost to follow-up (6%) were inserted in the analyses as censored data.

The pattern of survival and local failure for the whole series were estimated by means of the product limit method[8] on the basis of a 10-year follow-up period.

Because QUART entered into the routine use mainly after the end of the randomized trial, the results of the analysis considering different subgroups have referred to a maximum of 7-year follow-up time. Furthermore, to enable comparison with reports in the literature, the results that referred to a 5-year follow-up time have been given also.

The joint effect of the prognostic variables on the force of mortality was investigated by means of multiple regression analysis.

Preliminary graphical analyses suggested that the proportional hazard assumption was not tenable. On the other hand, the plots of log odds (probability of surviving/probability of dying) against log time for all the categories of prognostic variables resulted in parallel straight lines. Therefore the role of each of these latter variables was investigated by resorting to a multiple log-logistic regression model.[9] This was suitable for fitting breast cancer data also in previous papers.[10-12]

In the log-logistic regression model each of the partial regression coefficients (β_i) (i = 1....p) is recognizable as the log/odds ratio and it is constant in time.[9]

For patients classified in two prognostic categories and having the same survival experience, the statistics exp (β_i) = ϑ_i is expected to be 1.0. For ϑ_i less than 1 (ϑ_i more than 1) patients classified in a given category have an odds of surviving lower (greater) than that of patients in the reference category.

Results

Overall Survival

At the time of the analysis the median follow-up was 72 months (range, 1 to 202 months): a total of 124 patients died from breast cancer and 35 from other causes.

The overall survival of the whole series is shown in Figure 1; the probability of surviving (with 95% confidence limits) at 5 and 10 years from surgery are estimated to be 0.91 (0.89 to 0.93) and 0.78 (0.74 to 0.82), respectively.

Survival according to factors such as patient age and site and size of the primary and nodal status was also calculated.

Age at surgery. Patients were divided into four age groups. Survival curves of the four groups are shown in Figure 2. Seven-year survival probability is 0.91 for patients aged 46 to 55 years, 0.87 for the group aged 36 to 45 years, while the youngest group, women younger than 35 years, and the oldest one, women older than 55 years, have slightly lower probability (0.81 and 0.80, respectively) (Table 2).

Site of primary carcinoma. Two thirds of the patients had a primary carcinoma situated in the outer quadrants. The survival rate according to the site of the primary carcinoma, *i.e.*, external and internal quadrants of the breast, is shown in Figure 3. The two subgroups of patients have a similar pattern.

Size of primary carcinoma. Forty-two per cent of the patients had a carcinoma of 1 cm or less in diameter, while 53% had a primary between 1.1 cm and 2 cm. In 5% of the cases, the exact size was not evaluable, although clearly described as less than 2 cm. The survival curves according to the size of the primary carcinoma are shown in Figure 4. The cumulative probability of survival tends to decrease with increasing dimensions; the 7-year survival probability is 0.84 in the category of 1.6 cm to 2.0 cm, 0.84 in the category of 1.1 cm to 1.5 cm, 0.87 in that of 0.6 cm to 1.0 cm, and 0.94 in that of less than 0.5 cm (Table 2).

Axillary node involvement. Nearly one third of the patients (390, or 32%) had metastases in the axillary nodes. The survival of the four categories according to the number of involved nodes is reported in Figure 5.

No difference was found between the patients without node metastases and patients with one node involved, while the patients with more than one metastatic node show lower survival probability.

The 7-year survival rate decreased from 0.86 in node-negative cases to 0.67 in cases with more than three nodes involved (Table 2).

Multiple regression analysis. The first model adopted in the multiple regression analysis included all the above-mentioned variables. Due to the fact that site of primary carcinoma did not show any significant effect, a reduced model, including only the three remaining prognostic factors, was adopted.

Table 3 reports the estimates of coefficients together with their 95% confidence limits. Each of them allows the effect of the corresponding variable on the survival experience after making allowance for that due to the other variables inserted in the model. It appears that a patient

FIG. 1. Cumulative Survival of the whole series of 1232 patients.

with a tumor larger than 1 cm bears a worse prognosis than a patient with a smaller tumor; in fact the odds ratio is 0.78 with a 95% confidence limit (0.64 to 0.95).

For a woman aged 46 to 55 years, the odds of surviving is 1.6 as compared to that of a patient who is less than 35 years (reference category), while the odds ratios for the remaining age groups of patients are not significantly different from 1.

Increasing numbers of involved axillary nodes appear to reduce the odds of surviving, with the best prognosis

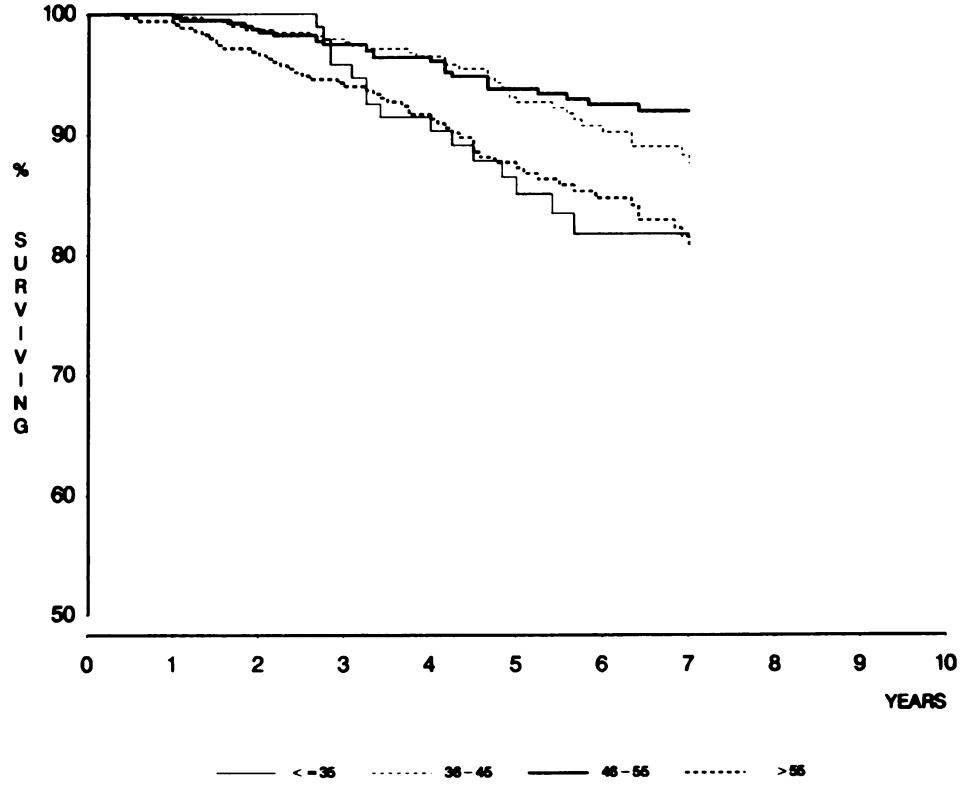

FIG. 2. Cumulative survival according to patient's age at diagnosis.

TABLE 2. *Five- and Seven-Year Survival of Patients, According to Age, Size of Primary and Axillary Node Metastases (95% Confidence Limits)*

Variables	Survival (%) At 5 Years	Survival (%) At 7 Years
Age (years)		
≤35	85 (77–92)	81 (73–90)
36–45	92 (89–95)	87 (83–91)
46–55	93 (91–96)	91 (88–94)
>55	87 (83–91)	80 (75–85)
Pathologic Size (cm)		
≤5	96 (92–100)	94 (89–99)
0.6–1.0 cm	93 (91–96)	87 (83–91)
1.1–1.5 cm	89 (86–93)	84 (80–89)
1.6–2.0 cm	84 (79–89)	84 (78–89)
Axillary Metastases		
No metastases	92 (90–94)	86 (88–91)
1 Node involved	91 (87–96)	89 (85–95)
2–3 Nodes involved	87 (80–94)	79 (69–90)
>3 Nodes involved	75 (65–86)	67 (54–80)

in node-negative patients (reference category). The odds ratio decreases with the increase of the number of involved nodes and it is significantly different from 1.0 for the patients with more than three involved nodes.

Unfavorable Events

Distant metastases. At the time of the analysis, a total of 171 patients had developed distant lesions. The cumulative probability of developing distant metastases at 5 and 10 years from surgery are estimated to be 0.12 (0.10 to 0.14) and 0.20 (0.17 to 0.23), respectively.

As in the analysis of survival, because the prognostic effect of tumor site was not statistically significant, the results of the multiple regression analysis presented in Table 4 concern three prognostic variables: age at surgery, tumor size, and axillary nodal status.

Women who are younger than 35 years (reference category) have the worst prognosis, and the odds ratios range from 1.99 (more than 55 years) to 3.0 (46 to 55 years) and are all significantly different from 1.0.

The odds of being free of metastases for a woman with a tumor measuring more than 1 cm is 0.73, as compared to that of a patient with a tumor measuring less than 1 cm. Increasing numbers of involved nodes appear to reduce the odds of being free of distant metastases, with the best prognosis in N- patients (reference category); odds ratios decrease with the increase of the number of involved nodes and it is not significantly different from 1.0 only for the patients with one involved node.

Ipsilateral recurrences and second tumors. Two possible local events may occur in the treated breast: local recurrence and second tumor. In our series of cases, no nodal recurrence in the axilla was recorded. Because it is difficult to distinguish between recurrences and new ipsilateral tumors, all patients who experienced a local unfavorable event were carefully analyzed by a joint team composed

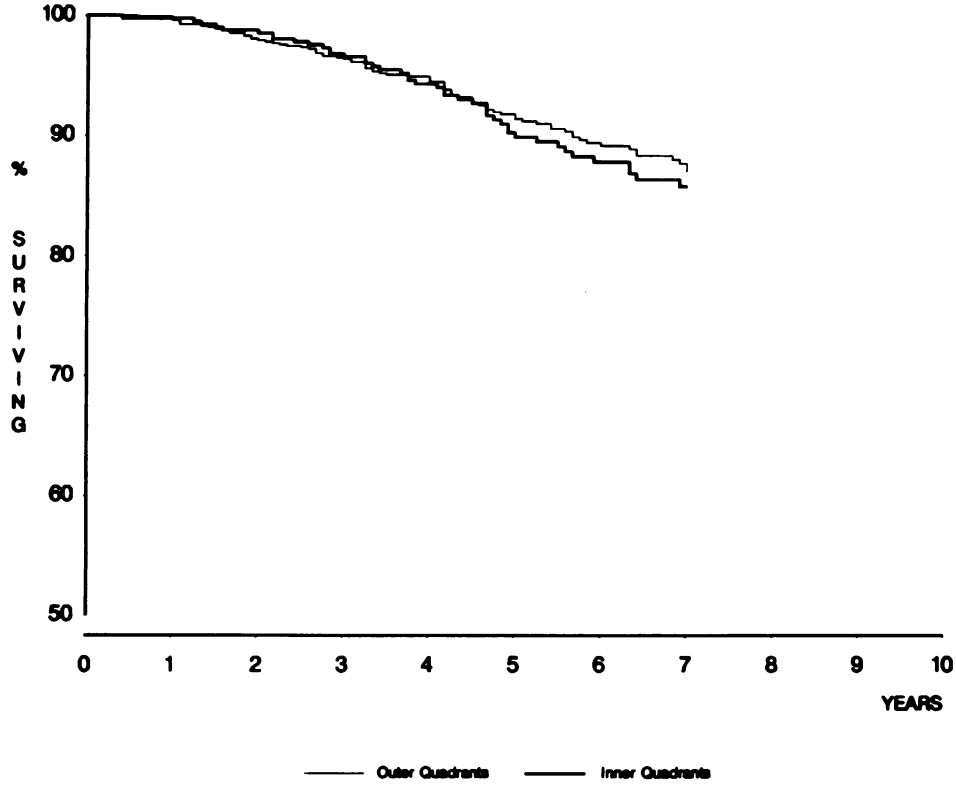

FIG. 3. Cumulative survival according to the site of primary carcinoma.

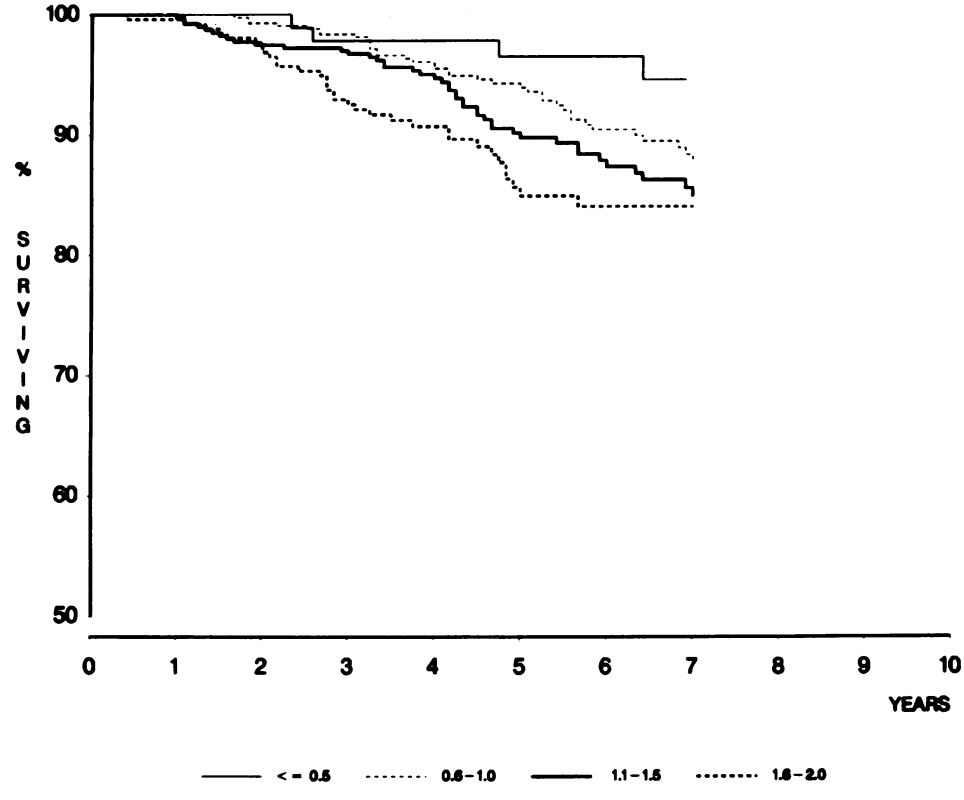

FIG. 4. Cumulative survival according to the size of primary carcinoma.

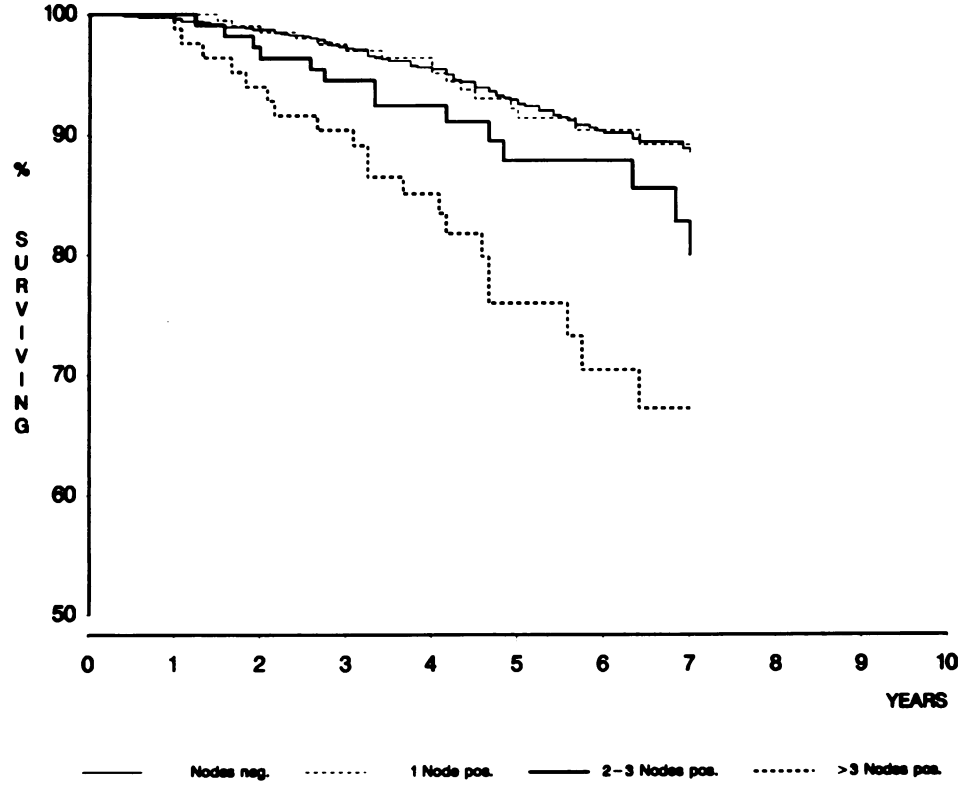

FIG. 5. Cumulative survival according to axillary nodes involvement.

TABLE 3. *Survival: Partial Regression Coefficients, Odds Ratios, and Their 95% Confidence Limits Estimated by Means of the Log-Logistic Regression Model*

Variables	β	Odds Ratio
Pathologic Size (cm)		
≤1 *vs.* >1	−0.25*	0.78 (0.63–0.96)
≤1 *vs.* not evaluable	−0.23	0.79 (0.53–1.21)
Age at Surgery (years)		
≤35 *vs.* 36–45	0.25	1.28 (0.90–1.82)
≤35 *vs.* 56–55	0.44*	1.55 (1.07–2.24)
≤35 *vs.* >55	−0.14	0.87 (0.62–1.23)
Axillary Nodal Metastases		
N− *vs.* 1 N+	−0.11	0.90 (0.68–1.19)
N− *vs.* 2–3 N+	−0.35*	0.70 (0.51–0.97)
N− *vs.* >3 N+	−0.89†	0.41 (0.30–0.55)

* <0.05.
† <0.01.

by a surgeon, a radiotherapist, a pathologist, and a diagnostic radiologist. The following criteria were used: nodules localized in the skin or the subcutaneous tissue were considered local recurrences, as were intramammary nodules located within 3 cm of the scar of previous surgery. Intramammary nodules located more than 3 cm away from the site of the primary tumors were defined as new primary carcinomas. According to these criteria, 35 local recurrences and 19 new primary ipsilateral tumors were recorded. The distribution of local recurrences, new ipsilateral primary carcinomas, and contralateral carcinomas, according to age, location of primary lesion, and axillary nodal status is showed in Table 5. The median time from initial surgery was 35 months (4 to 170 months) for local recurrences, 58 (21 to 131 months) for ipsilateral tumors, and 41 (3 to 160 months) for contralateral tumors.

Figure 6 shows the cumulative probability of developing a local recurrence, a second ipsilateral tumor, or a contralateral tumor as a function of time.

Patients presenting with recurrences or secondary recurrences in the breast were usually treated with total mastectomy. In 11 cases, however, it was possible to remove the tumor mass with a new wide resection. Of 35 women who underwent second surgery for local recurrences, 5 died from the disease (after 9, 11, 14, 28, and 87 months from relapse, respectively) while 30 are alive with no evidence of disease (follow-up time after relapse: median, 28 months; range, 1–109 months).

TABLE 4. *Distant Metastases: Partial Regression Coefficient, Odds Ratios, and Their 95% Confidence Limits Estimated by Means of the Log-Logistic Regression Model*

Variables	β	Odds Ratio
Pathologic Size (cm)		
≤1 *vs.* >1	−0.31*	0.73 (0.56–0.96)
≤1 *vs.* not evaluable	0.09	1.09 (0.58–2.09)
Age at Surgery (years)		
≤35 *vs.* 36–45	0.90†	2.45 (1.61–3.77)
≤35 *vs.* 46–55	1.09†	2.96 (1.92–4.58)
≤35 *vs.* >55	0.66†	1.94 (1.27–2.96)
Axillary Nodal Metastases		
N− *vs.* 1 N+	−0.20	0.82 (0.56–1.20)
N− *vs.* 2–3 N+	−0.73†	0.48 (0.32–0.72)
N− *vs.* >3 N+	−1.59†	0.20 (0.14–0.30)

* <0.05.
† >0.01.

TABLE 5. *Distribution of Local Recurrences (35), New Primary Ipsilateral Carcinomas (19), and Contralateral Carcinomas (45) According to Age and Size of Primary Carcinoma and Axillary Node Status*

Variables	No. of Local Recurrences	No. of New Ipsilat. Carcinomas	No. of Contralat. Carcinomas
Age at Surgery			
≤35	6	3	6
36–45	12	13	12
46–55	9	2	14
>55	8	1	13
Pathologic Size (cm)			
≤0.5	0	2	4
0.6–1.0	10	5	14
1.1–1.5	10	6	15
1.6–2.0	10	4	7
Not evaluable	5	2	5
Axillary Metastases			
No metastases	27	17	36
1 Metast. node	4	0	5
2–3 Metast. nodes	1	1	2
>3 Metast. nodes	3	1	2

Comparison of Patients In and Out of Trial

Of 1232 patients, 352 had been part of a clinical trial comparing the QUART technique to Halsted mastectomy; the overall survival of the whole series (352 in and out of trial) is depicted in Figure 7. Among the 880 cases, 769 patients were identified whose clinical and pathologic characteristics were comparable to those that had made the 352 cases eligible. These cases have been defined as superimposable. The other 111 cases were not considered superimposable, either because of different age (more than 70 years), or because of clinical stage (clinically positive axillary nodes).

A multiple log-logistic regression model was fitted to compare the overall survival and the distant metastases relapse patterns of patients treated in trial to the corresponding ones treated out trial, after adjusting for the three prognostic variables already commented on in the previous sections. With both responses no statistically significant difference emerged. By adopting in-trial patients as the reference category, the odds ratios are 0.96 (0.76 to 1.20) for survival and 0.86 (0.64 to 1.15) for distant relapse.

Oncogenic Risk of Radiation

Because all patients received radiotherapy on the operated breast (60 Gy), some scattered radiation reached

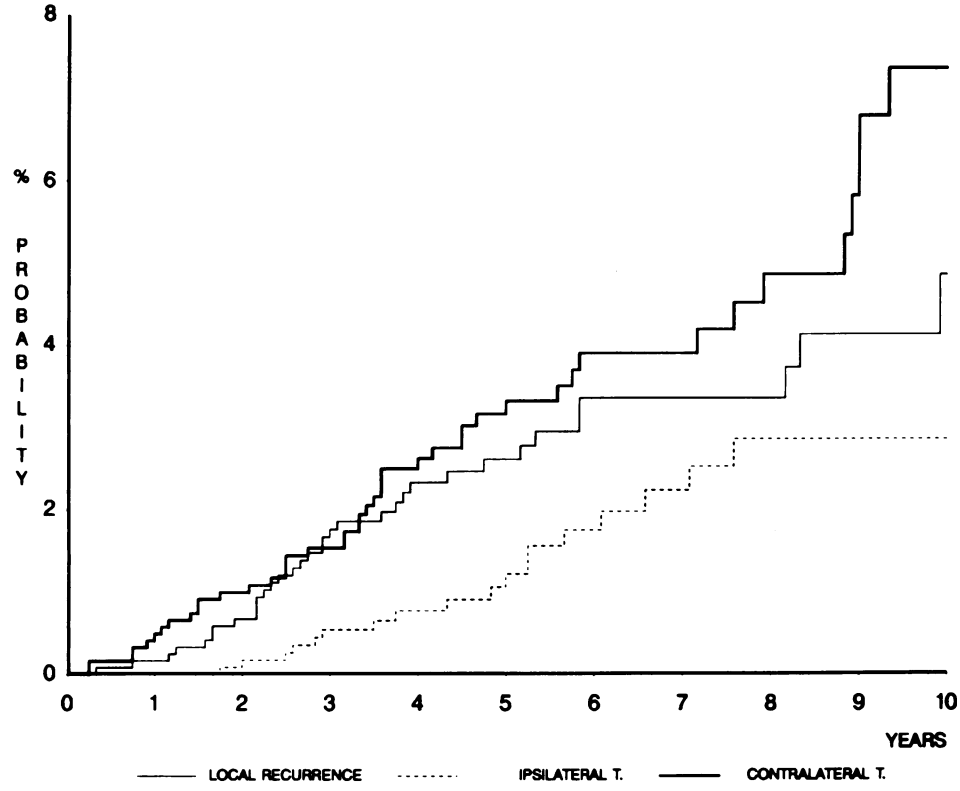

FIG. 6. Cumulative probability of local recurrences, second ipsilateral tumor, and contralateral tumor.

the contralateral mammary tissue. The quantity of radiation to the different portions of contralateral breast varies, being much higher for the inner one half of the breast.[13] Because the oncogenic effect of radiation is proportional to the dosage, one would expect an increased number of new primary mammary carcinomas in the heavily irradiated breasts compared to the number of primary carcinomas appearing in the contralateral breasts.

Our series shows, on the contrary, that 19 primary carcinomas appeared in the ipsilateral irradiated breasts, while 45 carcinomas occurred in the contralateral breasts. Moreover the distribution by site of those 45 cases does not show an increased incidence at the inner quadrants.

Discussion

The long-term survival curves of the 1232 cases of breast carcinoma of less than 2 cm in size treated with quadrantectomy, axillary dissection, and radiotherapy reconfirm that the outcome of this conservative approach is good, as was already shown by our early randomized clinical trial.[2,3] A source of indirect evidence that the QUART procedure is not inferior to mastectomy in terms of survival rates is the identity of the curves of the patient series treated inside and outside the clinical trial. This result shows that the QUART technique applied as a routine procedure in early breast cancer can achieve the same results obtained in patients treated within a clinical trial. This eliminates the doubts that sophisticated conservative procedures may give good results inside an investigational program (due to the optimization of all procedures and the choice of the best surgeons and radiotherapists), but may be risky when extended to the normal routine activity.

As regards the prognostic significance of patients' age, young women (those younger than 30 to 35 years) seem to have a worse prognosis than older women in terms of distant metastases. As far as overall survival is concerned, it appears that patients aged 35 years or less have a prognosis worse than that of patients aged 46 to 55 years, but not significantly different from that of patients aged 55 years or older. This finding might reflect the different pattern of general mortality of these age groups. In fact a poorer outcome of the treatment had already been shown in two previous papers of ours[14,15] for women under 40 years; the survival rate was definitely lower than that of

TABLE 6. *Treatment of Patients who Had a Local Recurrence, a New Ipsilateral Carcinoma, and a Contralateral Carcinoma*

	Number	Total Mastectomy	Breast Resection ± RT
Local recurrences	35	28	7
Second ipsilat. carcinomas	19	15	4
Contralateral carcinomas	45	17	27

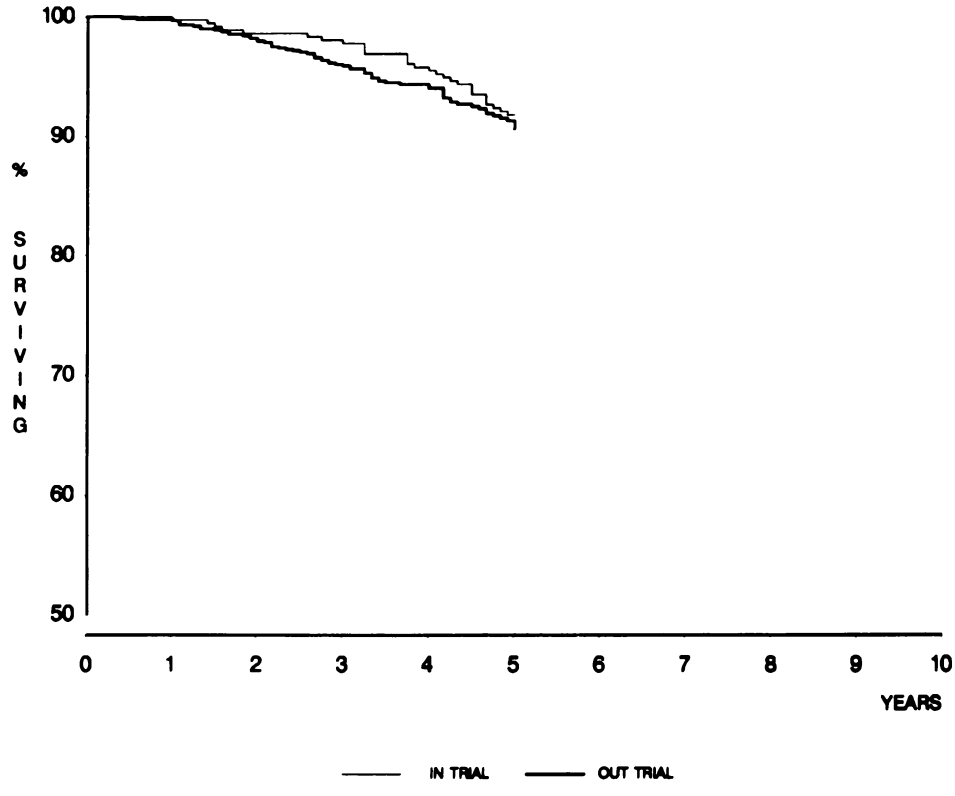

FIG. 7. Cumulative survival in patients treated inside a controlled randomized trial and in patients treated routinely.

older women, even for the N- subgroups. However it should be noted that the impact of age on survival rate is controversial. Some reports in the literature[16-19] and our recent study of 137 women[20] showed no difference in prognosis between young and older women. However it is difficult to compare the latter study to the present one because it concerned women of a more selected subgroup (20 to 30 years old) collected through a long period of time (14 years) and treated with a large variety of operations.

It is debatable whether tumor site is related to survival rate. In the present series of cases, no difference was recorded between the two subgroups of patients with tumors situated in inner or outer quadrants of the breast. The same conclusions had emerged from a previous study on 743 consecutive cases of breast cancer that were surgically treated.[14] This point seems to stress the futility of a more aggressive approach to tumors that are situated medially.

Obviously the larger the tumor the worse the prognosis, especially as it relates to the risk of local failure. The results of the present study seem to demonstrate that, within the limits of 2 cm in major diameter, there is no significant difference in survival between minimal tumors (those that measure less than 0.5 cm) and those that are 2 cm. When related to tumor size to nodal axillary metastatic involvement, it should be considered that even minimal cancers, measuring less than 0.5 cm, bear a relatively high risk of nodal metastases—21.5% according to our previous study[21] of 88 invasive microcarcinomas. This is a reason more in favor of a complete axillary dissection.

It was not a surprise to record, in our series, the differences in survival for subgroups according to nodal status and to the number of involved nodes. It is well known that the number of involved nodes is the most relevant factor in the assessment of prognosis.[22-24] In the present series, there was almost no difference in survival between node-negative women and those with only one node effected. Could this result be due to adjuvant chemotherapy? It is actually difficult to answer this question. In fact, adjuvant chemotherapy could have exerted a major effect in the presence of a minimal residual disease, but a conclusion of this type would appear to be inappropriate in this context because the data was retrospective.

The low rate of local recurrences after QUART represents an interesting and remarkable result. Only 35 women of 1232 (2.8%) experienced a recurrence of the removed primary tumor. The criteria according to which this lesions were distinguished from second tumors were previously described. Even when considering as a whole the recurrences and second-tumor rate, this would account for 4.3% of the total, a lower rate than those reported in the literature from two similar controlled studies, with rates of 6%[4] and 7.7%[5] at 5 years. The local recurrence rates after QUART or similar conservative procedure are not higher than those reported for patients with early cancers treated by radical traditional surgery.[3,4] Furthermore,

because only 5 women died of the 35 who underwent second surgery, it seems that local recurrences after QUART do not affect distant survival to the same extent as recurrences after traditional surgery do.

The incidence of second tumors in the irradiated breasts, 1.5% of the total, lower than that observed in the contralateral breasts, allows the conclusion that, at least within 10 years from the treatment, heavy irradiation of the breast does not increase the risk of new cancers.

Present results prove that it is time to abandon any doubt about the safety of conserving treatments for breast cancer of small size. This does not mean that any question on the subject has been answered. On the contrary, the problem of local recurrences and second tumors represents a stimulating challenge. A more precise knowledge of risk factors for local failures and new ipsilateral tumors would be very useful to better tailor the indications to limited, nonmutilating treatments. A thorough analysis of local unfavorable events observed in our total series of cases, treated in 1988, is in progress at the National Cancer Institute, Milan.

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